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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,967	04/07/2000	MATS WAHLGREN	45300-59676	4801

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EXAMINER
SMITH, LYNETTE F

ART UNIT	PAPER NUMBER
1645	18

DATE MAILED: 10/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary

Application No.	Applicant(s)
09/508,967	Wahlgren et al
Examiner	**Art Unit**
Lynette R. F. Smith	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 28, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *13-15, 17, 21, 24, and 33-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *13-15, 17, 21, 24, and 33-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). 17
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The examiner acknowledges the after final amendment filed 5/28/02. The amendment will be entered. Upon further consideration by the examiner, the finality of the last office action is being withdrawn. Claim 16 has been canceled. Claims pending and under consideration are claims 13-15, 17, 21, 24 and 33-38.

2. Upon further consideration by the examiner, all previous rejections under 35 USC 103 have been withdrawn.

3. The disclosure is objected to because of the following informalities: on pages 31-34 there are sequences which lack sequence identifiers. The sequence identifiers should be included with each sequence. Appropriate correction is required.

4. The use of the trademarks on pages 34 and 35 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

REJECTION MAINTAINED

5. The rejection of claims 13-15, 17, 33-38 under 35 USC 102(a)as being anticipated by Rowe et al is maintained for reasons set forth in paper no. 10, paragraph 4 of the previous office action.

Applicant urges that the polypeptide of Rowe et al is distinct from the claimed because the polypeptide of Rowe et al did not exhibit disruption of rosettes after heparinase treatment.

It is the examiner's position that Rowe et al disclose the expression products from two clones, one R29R+ and the other R29R-. The R29R- clone expressed polypeptides that were non-rosetting. It would follow that non rosetting clones would not be affected by heparinase treatment and rosetting clones would be effected by heparinase treatment. The polypeptide expressed by the R29R+ clone (rosetting polypeptide) is the same as the claimed polypeptide. Characteristics such as capability of binding a negatively charged heparan sulphate or heparan sulphate-like molecule as well as the partial amino acid sequence and molecular weight would be inherent in the expression product of the prior art. Additionally, it should be noted that the recitation of medicament, pharmaceutical or vaccine is being viewed as intended use which carries little patentable weight to the product. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

NEW GROUNDS OF REJECTION

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall c ntain a written description f the invention, and of the manner and pr cess of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 24, 33, 34 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide which binds to heparan sulphate or heparan sulphate-like molecules and a method for determining the rosette binding region utilizing the polypeptide, does not reasonably provide enablement for a pharmaceutical, vaccine or medicament comprising the polypeptide or any amino-terminal part of the polypeptide of seq. I.D. no. 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims are drawn to a pharmaceutical composition, a medicament or a composition, in a vaccine. The specification teaches the identification of a polypeptide termed PfEMPI which is useful as a receptor for malaria erythrocyte membrane protein. The specification fails to teach how the polypeptide or fragment of the polypeptide was used in a pharmacetical, vaccine or medicament. There are no animal models to show that the polypeptide indeed prevented or treated infection in patients. The development of vaccines and treatment therapies for individuals infected with malaria has been hampered by the fact that there is still no vaccine to prevent malaria. Baruch et al point out (WO 96/33736) that antibodies raised against a particular parasite will only react by parasitized erythrocyte (PE) agglutination with PE from the same strain (page 3). Studies have also shown that the malaria parasite exhibits variant surface antigens in different geographical locations hampering effective development of vaccine and treat

therapies. Without clear evidence showing the utility of polypeptides from malaria erythrocyte membrane proteins to protect against malaria, one of skill in the art would not readily know how to use the polypeptides for prevention without undue experimentation. Therefore in view of all of the above and in view of the state of the art, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claimed subject matter.

7. Claims 13-15, 17, 21, 24 and 33-38 are rejected under 35 USC 112 first paragraph because the specification, while being enabling for a polypeptide which binds to heparan sulphate or heparan sulphate-like molecules and a method for determining the rosette binding region utilizing the polypeptide, does not reasonably provide enablement for a polypeptide comprising any part of seq. I.D. No. 1. The claims are drawn to a polypeptide comprising an amino terminal part of seq. I.D. No. 1 or various amino acids of seq. I.D. No. 1, a vaccine, a pharmaceutical or a medicament comprising a part of seq. I.D. No. 1. The specification lacks guidance to show which part of the amino terminus of seq. I.D. no. 1 would have the claimed activity or which 400, 500 or so amino acids would have the claimed activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge of and

guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is **not** routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

The specification does not support the broad scope of the claims which encompass all modifications and fragments because the specification does **not** disclose the following :

- an amino acid sequence for the claimed protein;

- the general tolerance to modification and extent of such tolerance;

- specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;

- what fragments, if any, can be made which retain the biological activity claimed and

- the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have **not** provided sufficient guidance to enable one of skill in the art to make and use the claimed protein in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the proteins structure and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). Therefore, in view of all of the above, it is determined that it would require undue experimentation to make and use the invention commensurate in scope with the claimed subject matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 13-15, 17, 21, 24, 33-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claimed subject matter. The claims are indefinite because it is unclear what applicant intends by the recitation of

" an amino terminal part of the sequence". It is unclear from the specification what residues are involved in this "amino terminal part". Claim 38 is indefinite because it is unclear what applicant intends by the recitation of the composition being in a vaccine because it is unclear what the metes and bounds are of vaccine as it relates to a composition. Clarification of the claims is required in order to obviate this rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless -**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

9. Claims 13-15, 24, 33-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Helmby et al, Infection and Immunity 61(1), 1993. The claims are drawn to a polypeptide from a malaria erythrocyte membrane protein comprising an amino terminal part of seq. I.D. No. 1 with the claimed capability. The claims are also drawn to medicaments pharmaceuticals and vaccines comprising the claimed polypeptide.

Helmby et al teach the isolation of a 28kd erythrocyte protein from Plasmodium falciparum malaria parasite (page 285). The protein was administered to rabbits in an effort to produce antibodies. The 28kd protein is the same as the claimed protein. Characteristics such as amino terminal part, the number of amino acids as well as the binding capability would be inherent in the protein of the prior art. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to

show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. It should be noted that the recitation of "vaccine" or "pharmaceutical" or "medicament" is being viewed as intended use. Additionally, Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SPE Lynette R. F. Smith whose telephone number is (703) 308-3909.

Any inquiry of a general nature may be directed to the receptionist at (703) 308-0196.

SMITH/lfs
October 8, 2002

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